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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,665	11/17/2003	Mark Selby	PP01635.007	5235

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,665	SELBY ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34, 42, 45, 66, 69, 77, 80-86, and 88-91* is/are pending in the application.

4a) Of the above claim(s) *80-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,42,66,77,85,86 and 89-91* is/are rejected.

7)☒ Claim(s) *45,69 and 88* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 34, 42, 45, 66, 69, 77, 80-86, and 88-91 are pending in the application.

2. In the prior action, the final action mailed on January 24, 2007, claims 34-37, 42-45, 66-69, 77, 80-91 were pending; with claims 80-84 withdrawn as to non-elected inventions; claims 45, 69, and 88-91 objected to, and claims 34-37, 42-44, 66-68, 77, and 85-87 rejected.

3. In the After-Final amendment of March 27, 2007, the Applicant amended claims 34, 42, 66, 77, 80, 83, and 85; and cancelled claims 35-37, 43, 44, 67, 68, and 87.

4. Currently, claims 34, 42, 45, 66, 69, 77,85, 86, and 88-81 are pending and under consideration.

5. In view of the New Rejections, the Finality of the prior action is withdrawn, and the present action is made Non-Final.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **(Prior Rejection- Withdrawn)** Claims 34-36, 42-44, and 66-68 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Major et al. (J Virol 69: 5798-5805- of record in the Nov. 2003 IDS) in view of Michalak et al., (J Gen Virol 78: 2299-2306), and further in view of Valenzuela et al. (Bio/Technology 3: 323-26- also of record in the Nov. 2003

IDS). The claims have been amended to require that the encoded fusion protein includes the sequence of SEQ ID NO: 7, or a sequence of at least 90% identity thereto. Because the indicated references do not teach the specific sequences found in SEQ ID NO: 7, the rejection is withdrawn.

8. **(New Rejection- Necessitated by Amendment)** Claims 34, 42, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Major et al. (J Virol 69: 5798-5805) in view of Michalak et al., (J Gen Virol 78: 2299-2306) and Valenzuela et al. (Bio/Technology 3: 323-26) as applied previously, and further in view of Ono et al. (Nuc Acids Res 11: 1747-1757), Choo et al. (PNAS 88:2451-55), and Chapman et al. Nuc Acids Res 19:3979-86). As indicated above, these claims have been amended to read on nucleic acids encoding a fusion protein having the sequence of SEQ ID NO: 7, or a sequence of at least 90% identity thereto (thereby permitting up to 53 amino acid modifications).

The teachings of Major, Michalak, and Valenzuela have been described previously. These references render obvious a nucleic acid encoding a fusion protein encoding a truncated E2 protein comprising residues 374-661 fused to the N-terminus of a HBV S antigen (SAg). However, while these references teach the making of such a nucleic acid encoding an E2/SAg fusion, the references do not disclose the specific sequences of the encoded proteins such that it can be demonstrated that they fall within the scope of the variants to SEQ ID NO: 7 that are encompassed by the claim. It is additionally noted that SEQ ID NO: 7 includes, in addition to the truncated HCV E2 protein comprising residues 384-661 and the HBV S antigen, a human tissue

plasminogin activation (tPA) signal sequence at the N-terminus of the fusion protein, which is also not disclosed by the previously applied references.

However, the teachings of Ono and Choo respectively demonstrate that the SAg and E2 sequences used in the fusion of SEQ ID NO: 7 were known in the art. In particular, Figure 3 (page 1753) of Ono teaches the sequence of the subtype adw SAg, which is identical to the SAg of residues 306-531 of SEQ ID NO: 7. Similarly, the disclosure of the Choo reference teaches an HCV polypeptide sequence where residues 374-661 of the HCV polyprotein (the region corresponding to the truncated E2 of Michalak) encompasses a sequence identical to residues 26-303 of SEQ ID NO: 7. Further, the Chapman reference also teaches a vector for the expression of heterologous proteins in mammalian cells. It would therefore have been obvious to those of ordinary skill in the art to use such a vector for the expression of the fusion suggested by the other references in such cells. Chapman teaches the use of the tPA signal sequence terminating with the two residues alanine and serine) in the vector. This sequence corresponds to residues 1-25 of SEQ ID NO: 7. See e.g., Golden et al., Protein Expr Purif 14: 8-12 (teaching on page 9, left column the coding sequence for the tPA signal sequence, which is identical to the bases of SEQ ID NO: 6 encoding the first 24 residues of SEQ ID NO: 7 as well as the first two bases encoding the 25th residue of SEQ ID NO: 7). Those of ordinary skill in the art would have had a reasonable expectation of success to substitute the HBV and HCV sequences of Ono and Choo for those in the previous references as the different sequences would represent functional equivalents of the viral sequences used in those references. Those of ordinary skill in the art would also have been motivated to use the vector of Chapman because the vector is disclosed as useful for the

expression of heterologous sequences, such as the fusion protein suggested by the other references.

The cumulative teachings of the prior art therefore render obvious a nucleic acid encoding a protein including residues 1-25 (the tPA signal) residues 26-303 (the E2 protein) and 306-531 (the SAg sequence) of SEQ ID NO: 7. The fusion suggested by the art would also include an additional 13 residues at the N-terminus of the HCV sequence (see, page 2301, Figure 1 of Michalak, showing the truncated E2 protein as comprising residues 371-661 of the HCV sequence) and would lack the two residue linker sequence (Ile-Asp) of residues 304 and 305 of SEQ ID NO: 7. However, the nucleic acid of the prior art would therefore encode a sequence varying from SEQ ID NO: 7 by only 15 residues, thus sharing at least 90% identity thereto.

Moreover, it was well known in the art to use linker and spacer sequences in the making of fusion proteins for multiple reasons (see e.g., U.S. 5,292,646, column 8). It would therefore have been obvious to those of ordinary skill in the art to include such a sequence between the HCV and HBV sequences in the fusion suggested by the prior art. Thus, the inclusion of such sequences at positions 304 and 305 would have been obvious to those of ordinary skill in the art. The specific residues chosen would therefore represent an obvious embodiment on the use of such a linker or spacer sequence.

The combined teachings of these references therefore render the claimed nucleic acids obvious.

9. **(Prior Rejection- Restated and Maintained)** Claims 77 and 79 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al. (U.S. 6,306,625), in view of Major,

Michalak, and Valenzuela as applied to claims 34-36, 42-44, and 66-68 above. Claim 79 has been cancelled from the application. Claim 77 has been amended in a similar manner to claim 34. I.e., the claimed cell line must now include a nucleic acid encoding SEQ ID NO: 7 or a sequence at least 90% identical thereto. In view of the amendment, the rejection is restated as a rejection of claim 77 over the teachings of Jacobs in view of Major, Michalak, and Valenzuela, and further in view of Ono, Choo, and Chapman as applied against claims 34, 42, and 66 above.

10. **(Prior Rejection- Withdrawn)** Claim 37 was rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs in view of Major, Michalak, and Valenzuela as applied to claim 77 above, and further in view of the teachings of and GenBank Accession Numbers X02763, and M62321. This claim has been cancelled from the application. The rejection is therefore withdrawn.

11. **(Prior Rejection- Restated and Maintained)** Claims 85-87 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs in view of Major, Michalak, and Valenzuela as applied to claims 77 above, and further in view of De Wilde et al. (U.S. 5,928,902), U.S. 4,722,840 (the 840 patent), and Mountford et al (PNAS 91: 4303-07). Claim 87 has been cancelled from the application. Claims 85 and 86 have also been amended to require that the encoded fusion protein includes SEQ ID NO: 7 or a sequence at least 90% identical thereto. In view of the amendment, the rejection is restated as a rejection of claims 85-87 over the teachings of Major, Michalak, and Valenzuela in view of Ono, Choo, and Chapman as applied above, and further in view of Jacobs, De Wilde, the 840 patent, and Mountford as applied previously.

12. **(New Rejection)** Claims 89-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Major, Michalak, and Valenzuela, in view of Ono, Choo, and Chapman as applied against claims 34, 42, and 66 above, and further in view of the teachings of Maertens et al. (6,890,737) or of Flint et al. J Virol 73: 6782-90). These claims are limited to embodiments of the prior claims wherein the nucleic acid encodes SEQ ID NO: 7.

As indicated above, the teachings of the previously described references render obvious nucleotide sequences encoding fusion proteins sharing at least 90% identity to SEQ ID NO: 7. In particular, the references suggest nucleic acids encoding fusions varying from SEQ ID NO: 7 only in the inclusion of a linker sequence at residues 304 and 305 of the fusion protein (the inclusion of which would have been obvious to those of ordinary skill in the art), and by the additional inclusion of residues 371-383 of the HCV polyprotein.

The teachings of Maertens indicate that it was known that the E2 protein begins at residue 384 of the HCV polyprotein. See e.g., column 3, lines 40-42. Further, like the Michalak reference, this reference also teaches truncated forms of this protein terminating at residue 661. Column 13.

The Flint reference provides similar teachings to the Valenzuela reference. In particular, this reference teaches fusion of the HCV E2 protein to another viral envelope protein such that the E2 protein is incorporated onto the surface of another virus-like particle. Abstract. Flint specifically teaches the successful expression and inclusion into such a particle a fusion of the truncated HCV protein comprising residues 384-661. Page 6784, Figure 1.

From either of these teachings, it would have been obvious to those of ordinary skill in the art to modify the teachings of the Major, Michalak, and Valenzuela references so as to include only the E2 coding regions, and thus result in a fusion protein comprising residues 384-661 of the HCV polyprotein.

The combined teachings of these references therefore render the claimed inventions obvious.

Conclusion

13. No claims are allowed. Claims 45, 69, and 88 appear to be allowable over the prior art. The prior art does not appear to teach or suggest the vector of SEQ ID NO: 6. However, these claims are objected to for depending on rejected claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner